REMARKS

Support for the Claim Amendments

Support for the claim amendments can be found throughout the specification and in particular on page 14, lines 18-24 (e.g., detecting the PAR-1 level, the PAR-4 level, or both); and page 12, lines 12- page 13, line 2 (e.g., reducing or inhibiting PAR-1 and/or PAR-4 levels).

Summary of Interview with the Examiner

The Applicant's attorney and Applicant conducted an in-person interview with Examiners Pagonakis and Fetterolf, on March 3, 2010. In accordance with the Interview Summary, the Applicant acknowledges that claim amendments were discussed. The specific claim amendments suggested by Examiners to overcome the art of record are being made herein. The Applicant's attorney and Applicant thank the Examiners for their time and consideration.

Claim Rejections - 35 U.S.C. §103

The Examiner rejected Claims 1, 5-10, 12, 14 and 22-23 under 35 U.S.C. §103(a) as being unpatentable over Birnbaum *et al* (Cardiovascular Drugs and Therapy, 17, 25-30, 2003) hereinafter "Birnbaum" in view of Kahn *et al* (Journal of Clinical Investigation, Vol. 103, No.6, 1999) hereinafter "Kahn".

The Examiner states that Birnbaum teaches a method of reducing myocardial infarction size in an individual comprising administering a dose of atorvastatin and with regards to the dose, Birnbaum teaches that the dose of atorvastatin is 10-75 mg/kg/d; however, the Examiner states that Birnbaum does not teach selecting a patient with elevated PAR-1 and PAR-4 levels. Furthermore, the Examiner states that Kahn teaches that platelet dependent arterial thrombosis underlies myocardial infarctions (page 879, column 1), and that it was demonstrated that PAR-1 and PAR-4 are functionally expressed in human platelets, and that these receptors account for most if not all thrombin signaling in these cells Page 885, column 1. Office Action, page 3. Thus, according to the Examiner, one of ordinary skill in the art would have been motivated to select patients with elevated PAR-1 and PAR-4 levels because the activated PAR-1 and PAR-4 activate thrombin which activated platelets which, in turn, is the underlying cause of myocardial infarction.

The Applicant respectfully disagrees and requests reconsideration. One of skill in the art would not combine Birnbaum with Kahn because there is no link nor suggestion in the cited art that statins inhibit or reduce PAR-1, PAR-4, or both levels as in the claimed invention.

The assessment of PAR-1 or PAR-4 levels as an indication of statin administration is surprising and unexpected. Although statins may have an effect on myocardial infarct size, there is no indication in the art that statins play a role with platelets. In fact, the inventor published a study in Archives of Internal Medicine, in which the interaction between Clopidogrel and statin was examined. *See* Reference AX5, Serebrauny, Victor L., MD, PhD. *et al.,Arch of Intern Med*; 164: 2051-2057 (2004). During this study, a number of platelet receptors were measured and a number of platelet receptors, when inhibited, did not have any effect on vascular disease outcomes. According to the Declarant, Table 2 shows the level of a number of platelet receptors in patients that received statins and those that did not. Also as shown in Table 2, statins had no effect on the platelet receptors, except PAR-1 and PAR-4. Hence, there was no expectation or motivation in the art that statins had an impact on a platelet receptor, and in particular on PAR-1 or PAR-4.

In fact, this finding was accidental. The Declarant states:

> In this study set forth in Reference AX5, we set out to assess the interaction between Clopidogrel and statins. We assessed a number of platelet receptors in patient groups that were taking statins and those that were not taking statins. Referring to Table 2, there was no statistical significance in any platelet receptor except PAR1 and/or PAR-4 in patients on statins and those not receiving statins. *The effect of statins on PAR1 and/or PAR-4 was surprising and unexpected. We made the observation accidently, when trying to solve a totally different problem*, namely to determine the interaction between Clopidogrel and statins. Declaration, paragraph 6, emphasis added.

Even the cited reference, Birnbaum, attributed the mechanism of action of PAR-1 and PAR-4 to eNOS (endothelial nitric oxide synthase) and not to platelets. No connection between platelet receptors, PAR-1 and PAR-4, was established until the discovery of the claimed invention. The selection of patients having an elevated level of PAR-1 and/or PAR-4, and to assess the need for

statin administration was not contemplated by a skilled artisan even in light of the cited references. The Declarant states:

> As an expert in the field of platelets, I would not have expected this association, namely that statins reduce PAR-1 or PAR-4 levels. Declaration, paragraph 5.

Furthermore, the Declarant states:

> During my many years studying platelets, as an expert, I could not have made the connection without the data that supports the claimed invention.
> Declaration, paragraph 7.

Applicant has amended the claims to further distinguish the claimed invention from the cited references, and specifically include the limitations suggested by the Examiner during the interview. These amended claims select a PAR-1 and/or PAR-4 patient population, and detect PAR-1 and/or PAR-4 levels after administration of a statin.

Accordingly, the amended claims and arguments overcome the 35 U.S.C. §103 rejections, and Applicant respectfully requests reconsideration.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is *encouraged* to call the undersigned.

Respectfully submitted,

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